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Background

Kaposi sarcoma (KS) flare (exacerbation) may occur following therapy with corticosteroids, as part of the immune reconstitution inflammatory syndrome seen with highly active antiretroviral therapy (HAART), and after rituximab therapy. The exact mechanism responsible for iatrogenic KS flare is unclear. Therefore, the aim of this study was to investigate the pathologic features in cases of AIDS-associated KS flare.

Methods

Two cases of AIDS-associated cutaneous KS flare were identified following rituximab therapy. Tissue biopsies obtained from these KS flare lesions were compared to similar controls (AIDS-KS samples of similar stage from patients who had not received rituximab) by means of immunohistochemistry using vascular makers (CD34, CD31), monoclonal antibodies to human Herpesvirus-8 (HHV-8) gene products (LNA-1, K5), as well as B-lymphocyte (CD20) and T-lymphocyte (CD3, CD4, CD8) markers.

Results

One patient was a 36-year-old male, HIV-positive for 2 years (CD4 T-lymphocyte count 363 cells/mm3; HIV viral load >100,000 copies/ml), and the other a 44-year-old male, HIV-positive for 5 years (CD4 T-lymphocyte count 443 cells/mm3; HIV viral load <75 copies/ml), who had both received rituximab therapy for multicentric Castleman disease. The former manifested with cutaneous KS after 7 days, and the later patient with skin and lymphadenopathic KS flares within 3 months of receiving rituximab. In the control cases both CD3 and CD20 cells were present, with a preponderance of T-lymphocytes identified. In the KS flare specimens, there were only T-cells present with a notable absence of B-lymphocytes. In all control and flare KS cases T-cell subsets showed CD8 > CD4. CD20+ B-cell depletion in the KS flare case of the 36-year-old patient occurred concomitantly with activation of the HHV-8 immediate early gene protein K5. KS flares in both patients were successfully treated with liposomal doxorubicin and valganciclovir.

Conclusion

Rituximab-induced KS flare appears to be related to a modification in the host immune system, most notably with complete absence of B lymphocytes in the KS lesion. B-cell depletion with rituximab in patients at risk for KS development may activate HHV-8, resulting in unwanted KS flare. Effective management of iatrogenic KS flare therefore depends upon the control of HHV-8 viremia in conjunction with specific chemotherapy for KS.